DETAILED ACTION

As a preliminary matter, the application has been transferred to Examiner Frank Choi, Art Unit 1616.

Drawings

The drawings are objected to because Figures 1, 3, 4 and 5 contain cross-section circles which are filled in which imply that the synthetic material is other than a monolithic material. Empty circles should be used instead. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

Specification, Page 11, "DESCRIPTION OF THE DRAWINGS" should be "BRIEF DESCRIPTION OF THE DRAWINGS".

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34, 36, 38,39, 41, 42, 49, 56, 57, 61, 64-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yafuso et al. (US Pat. 5,583,213) in view of Shah et al. (US Pat. 6,248,127), Sahatjian et al. (US Pat. 5,135,516) , WO 97/41164, WO 0013719, Guire et al. (US Pat. 5,512,329) and Hsu et al. (US Pat. 5,417,969).

Yafuso et al. disclose that surfaces of medical devices that are in direct contact with biological materials, such as tissues, blood and blood products, have been treated with surface modifying agents, such as sulfated polysaccharides, in order to make the contacting surfaces compatible with these types of sensitive biological materials (Column 1, lines 15-21). It is disclosed that catheters and tubing may be treated with biologically active polysaccharides to make the surfaces of such devices nonthrombogenic (Column 1, lines 21-28). It is disclosed that the polysaccharides are activated by combining the polysaccharide with a tetraalkylammonium hydroxide, where the polysaccharide can be heparin, heparan sulfate, chondroitin sulfate, dermatan sulfate, fucoidin sulfate, dextran sulfate or keratin sulfate (Column 2, lines 35-68, Column 3, lines 1-33). It is disclosed that the activated polysaccharides are coupled to at least

one exposed surface of a suitable polymeric or metal substrate or support, in which the materials are in the form of shaped articles, films, fibers and devices such as vascular grafts, catheters, cannulas, stents, etc. (Column 4, lines 15-53). It is disclosed that the polymeric substrates can include polyalkylenes, polycarbonates, polyurethanes, polyesters, polyfluoropolymers, silicones, polyamides, etc. (Column 4, lines 33-40). It is disclosed that polysaccharide ammonium salt is converted into an activated agent by using a suitable coupling agent in an aprotic polar organic solvent such as dimethylsulfoxide (Column 5, lines 45-64).

Shah et al. disclose that heparin quaternary ammonium complexes typically leach away from the substrate to which they are applied in a few hours (Column 1, lines 54-68). It is disclosed that by combining the heparin complex with a silane prior to coating of the substrate, the coating has superior durability compared to known coatings and does not require a base/primer layer (Column 3, lines 1-60). It is disclosed that coated medical devices included stents and catheters (Column 6, lines 3-15). It is disclosed that the coatings are preferably prepared using an organic solvent, such as tetrahydrofuran, however, water can be used in the preparation of the coating (Column 4, lines 50, 51, Column 6, lines 27-38). It is disclosed that the coatings can include a film forming agent dissolved simultaneous with the silane, including acrylic polymers (Column 6, lines 15-26).

Sahatjian et al. disclose an antithrombogenic coating where heparin is electrostatically bound to quaternary ammonium which coating can be used on cathethers, guidewires, mechanical heart valves, vetricular assist devices, implantable artificial hearts, vascular grafts, etc. (See entire document, especially, Columns 1, 2, Column 3, lines 1-35). It is disclosed that heparin and ammonium cation are applied in a manner that heparin is bound by electrostatic

attraction to the ammonium cation to permit time release of heparin and that the ammonium cation may be applied before the heparin is applied (Column 1, lines 55-68, Column 2, lines 1-20). It is disclosed in various embodiments the polymer may contain ammonium salts, acid salts having cations other than ammonium cation and, sodium salts of the acid (Column 3, lines 1-5).

WO 97/41164 discloses heparin can be in the form of a heparin monomer in which heparin is linked to a polyoxyalkylene methacrylate or polyoxyalkylene acrylate through an ester or carbonate linkage (Page 11).

WO 0013719 discloses that heparin can be combined with a carrier to effect the immobilization of the heparin on the surface of a medical device and that said carrrier can include organic compounds carrying functional groups such as amino, aldehydo, hydroxyl, carboxylic acid, carbodiimido or other reactive functional groups that can be bound to functional groups present in or introduced into the heparin, including benzalkonium chloride derivatives and polycarboxylic acids and polyalcohols and other functional polymers or combinations thereof (Page 8, lines 4-17). It is present that the functional groups are present in such an extent and that a sufficient amount of heparin can be bound and a strong antithrombogenic activity can be obtained (Page 8, lines 15-18).

Guire et al. discloses that polymer molecules and reactive monomers can be provided with latent reactive groups covalent bonded to that when the molecules are brought into bonding proximity with a substrate the latent reactive groups can be energized to form bonds between the molecules and the substrate, which avoids the necessity of pretreating the substrate and enables the molecules to be attached to substrates of varying types (Column 1, lines 45-58). It is disclosed that the polymers molecules can include polysaccharides, such as heparin (Column 3,

lines 1-34). It is disclosed that the latent reactive groups are responsive to ultraviolet, visible or infrared portions of the electromagnetic spectrum and include azides (Column 4, lines 3-25).

Hsu et al. disclose the use of ionizing radiation to bond the organic cation-heparin complex to the polymer, which radiation also serves to sterilize the coated polymeric material (Column 7, lines 5-68, Column 8). It is disclosed that in an alternative embodiment, once the organic cation-heparing complex is bound to polymer by ionizing radiation, the organic cation can be replaced by cation having a higher degree of biocompatibility by contacting the coated surface with an liquid solution having an ionic strength sufficiently high to exchange organic cations with a cation in the liquid; for example, a 20wt% solution of NaCl (Column 9, lines 19-57). It is disclosed that it is speculated that the radiation causes free radicals to form on both the polymeric material and heparin which combine to form a covalent bond with the amount of radiation varying depending on the type of polymeric material and amount of heparin coating (Column 10 lines 13-21).

The prior art discloses coating of medical devices, such as catheters and stents, with quaternary ammonium polysaccharide complexes. The difference between the prior art and the claimed invention is that the prior art does expressly disclose tubular medical devices coated with quaternary ammonium polysaccharide complexes which complex additionally contains at least one functional group capable of forming a covalent bond and is prepared in an organic solvent, where the polysaccharide is first combined with the functional group before complexing with the quaternary cation. However, the prior art amply suggests the same as the prior art disclose the combination of heparin quaternary ammonium complexes with silanes and other film formers prepared in an organic solvent, such as tetrahydrofuran, that the heparin combined

with a carrier which combines quaternary ammonium compounds and polymer functional groups, that polymers, including heparin, can be modified with reactive groups, such as azides, reactive to electromagnetic radiation, that quaternary ammonium is bound to heparin electrostatically, that polysaccharide ammonium salts can be activated by combining with a coupling agent in dimethylsulfoxide and that quaternary ammonium ions can be removed from the polymer by exposing with a sodium chloride solution . As such, one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the combination with silanes would result in a coating that is more durable than quaternary ammonium polysaccharide complex alone in terms of leaching of the quaternary ammonium polysaccharide complex and that various methods of preparation would be suitable, including the use of organic solvents, such as tetrahydrofuran and dimethylsulfoxide, combining heparin with a monomer or monomers having a functional group or groups before or after combination with the quaternary ammonium compound, combining with azides which are sensitive to electromagnetic radiation, and removing the quaternary ammonium ion with a sodium chloride solution, with the expectation that the medical device would have an anti-thrombogenic activity, that use of electromagnetic radiation and sensitive reactive groups would help to fix heparin complex onto the substrate and sterilize the substrate at the same time, that the heparin will bound in part to the substrate electrostatically via the electrostatic bond with the quarternary ammonium compound which combination is coated onto the substrate and that removal of the quarternary ammonium ion with sodium chloride solution would result in a more biocompatible medical device.

The Examiner has duly considered the Applicant's arguments but deems them moot in light of the new grounds of rejection herein.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Thursday, Friday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
June 10, 2008

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616